CONGENITAL ECTROPION AND DISTICHIASIS

ETIOLOGIC AND HEREDITARY FACTORS: A REPORT OF CASES AND REVIEW OF THE LITERATURE

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Congenital ectropion and distichiasis, more especially the former, are anomalies of the eyelids to which the much abused term "rare" can properly be applied.

ECTROPION

Most textbooks either do not mention the congenital variety of ectropion at all or devote little space to it. Duke-Elder (1), for instance, describes secondary eversion of the lid margins as a congenital phenomenon associated with microphthalmos and buphthalmos and secondary eversion of the lower lids associated with orbitopalpebral cysts but notes that primary ectropion is very rare indeed. Sorsby (2) mentions the possible existence of congenital entropion in his detailed and extensive presentation of congenital anomalies of the eyes and adnexa. Mann (3), after noting that both entropion and ectropion are exceedingly rare as congenital defects, says of ectropion that it involves the upper eyelids more often than the lower and may be associated with either an abnormality or complete absence of the tarsal plate. If the lower lid is involved, she continues, microphthalmia is usually present, associated with an orbital cyst. If the upper lid is involved, there may be a deformity of the skull; her reason for the last statement, which is not borne out by the recorded cases, is not apparent.

An exhaustive review of the literature (including, as a precaution, the literature of congenital entropion) has revealed only twelve recorded cases of congenital ectropion. These few reports do not make clear the anatomic factors involved in the production of this anomaly, nor do they pay particular attention to the role of the gene as an etiologic factor. There are, in fact, few clear-cut statements in these papers about

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the direct causation of congenital ectropion, some writers apparently failing to realize that it is the expression of a variety of causes rather than a single pathologic entity.

To clarify this confused situation, the following etiologic classification is suggested:

1. Congenital ectropion due to absence or anomaly of the tarsus.
2. Congenital ectropion (congenital eversion of the eyelids, the nomenclature suggested by Ostriker and Lasky [4]) due to eversion of the eyelids during passage through the birth canal.
3. Congenital ectropion due to changes in the skin of the lids, such as would be associated with hyperkeratosis or icthyosis congenita.
4. Congenital ectropion due to microphthalmia and orbital cysts.

Groups 1 and 2 represent true primary congenital ectropion. Groups 3 and 4, in which both causative factors and diagnosis are usually clear-cut, represent the secondary congenital variety.

DISTICHIASIS

The literature on congenital distichiasis, although it is considerably more extensive than the literature on congenital ectropion, is still scanty, and in only a few reports is it mentioned that congenital ectropion and congenital distichiasis may coexist.

After encountering a case of combined congenital ectropion and distichiasis, I found myself fortunate enough to be able to study three generations of the patient's family, including her own; most of the members could be examined personally. Ten of the patient's relatives suffered from congenital ectropion and nine from distichiasis, either as an isolated entity, or, in seven cases, in combination with ectropion.

This remarkable concentration of cases in a single family provided an opportunity, apparently not previously available, to study the probable mode of inheritance of congenital ectropion and congenital distichiasis. The microscopic studies carried out in two cases also made it possible to implicate a defect of the tarsus as a possible causative agent in congenital ectropion.

CASE STUDIES

This investigation, which took place in Puerto Rico, was stimulated by the observation of an eighteen-year-old girl (hereafter called the propositus) who showed marked ectropion of both lower eyelids associated with distichiasis of the upper eyelids. When questioning revealed that many of her ancestors and living relatives apparently presented

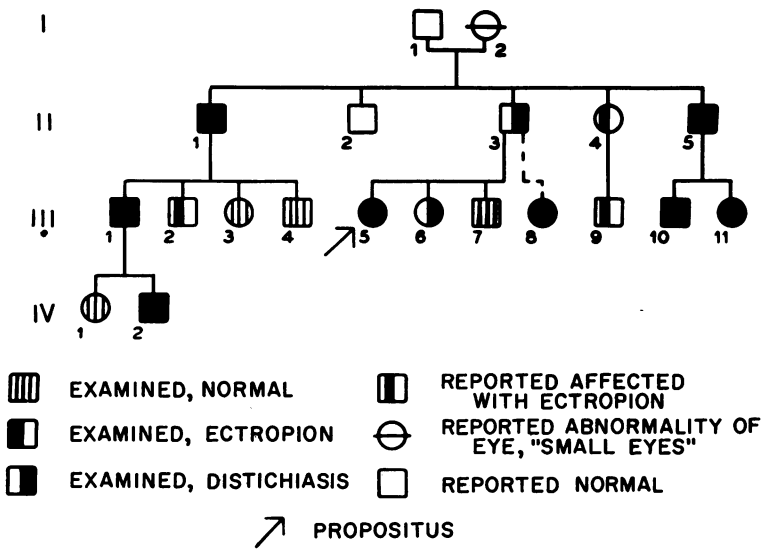

FIGURE 1. OCCURRENCE OF CONGENITAL ECTROPION AND DISTICHIASIS IN FAMILY OF TWENTY MEMBERS

similiar anomalies, a detailed study was undertaken of all members of the family.

The investigation (Figure 1) revealed nineteen relatives of the propositus, in four generations, four of whom were dead. Thirteen of the fifteen living relatives were personally examined, and information about the other two was obtained from Dr. Edmund B. Spaeth, who had operated on them.

Although there was no history of consanguinity in the family, the spouses of the married members were included in the investigation. As examination revealed no evidence of ectropion or distichiasis in any of them, they are omitted from the record except for the (deceased) grandfather of the propositus (generation I, 1), who is included to complete the chart. It was reported that his eyes were normal.

The (deceased) grandmother of the propositus (I, 2) was said to have had the same type of "small" eyes seen in several living members of the family. In the next generation, a boy (II, 2), who had died at the age of seven years, apparently had normal eyes. A female in this generation (II, 4), who had died at the age of thirty-five years, had apparently had an extreme ectropion of all four eyelids since birth; no information was available about a possible distichiasis in this case.

The routine examination in the fourteen members of this family

examined personally consisted of external examination and ophthalmoscopy, usually accompanied by refraction. Special studies consisted of (1) inspection of the position and appearance of the eyelids; (2) palpation of the lids to determine the condition of the tarsus; (3) investigation of the margin of the eyelids, including slit-lamp examination, with a special search for aberrant eyelashes and the openings of the meibomian glands; (4) determination of the length of the palpebral fissure; (5) determination of the height and vertical extension of the upper eyelids by Fuchs's technique; (6) a study of the conjunctiva; (7) a study of the cornea for opacities; (8) tonometry.

The case histories which follow, as well as the case reports from the literature, include only the findings important in relation to ectropion and distichiasis. Unimportant and irrelevant negative findings are not included.

CASE 1 (III, 5; Figure 2). This eighteen-year-old white girl, the propositus, was first seen December 31, 1952, with a history of ectropion of the lower eyelids since birth. She complained of photophobia and irritation of both eyes. On questioning, she stated that several other members of her family suffered from the same condition.

Examination showed complete ectropion of both lower eyelids, easily corrected by pulling the temporal third of the lids up and out. The skin was loose and flaccid but otherwise normal in appearance. There was no evident shrinkage of the subcutaneous tissues, but on palpation the tarsus could not be demonstrated and the lids seemed thinner than normal. Vertical extension of the lower lids from the lower border of the orbit to the border of the replaced lids was apparently normal.

Function of the orbicularis muscle in both lids on both sides seemed normal, but when the girl was told to close her eyes, as if she were asleep, closure was not complete and the lowermost portion of the cornea and a portion of the eyeball were left exposed.

The lower eyelashes were in normal position at the anterior border of the lid margin, but they were much smaller, thinner, and paler, as well as less numerous, than the upper eyelashes. The openings of the meibomian glands could not be seen in either upper or lower lid, and no lashes were found at the posterior border of the margin of the lower lids, where the meibomian orifices are normally present.

The upper eyelids were normal in position and apparently normal tarsi could be demonstrated. The anterior row of eyelashes was normal, but on each upper lid, just above the outer canthus and very close to the posterior border of the lid margin, was a bunch of eight or ten apparently normal cilia. Close to the lacrimal punctum on each upper lid, also near the posterior border of the lid margin, were three rather small eyelashes.

The palpebral fissures were narrow horizontally. The following measurements of the upper lids were secured by Fuchs's (5) technique: right upper eyelid: length 18 mm., vertical extension 25 mm., coefficient, 1.39; left upper eyelid: length 20 mm., vertical extension 27 mm., coefficient 1.35.

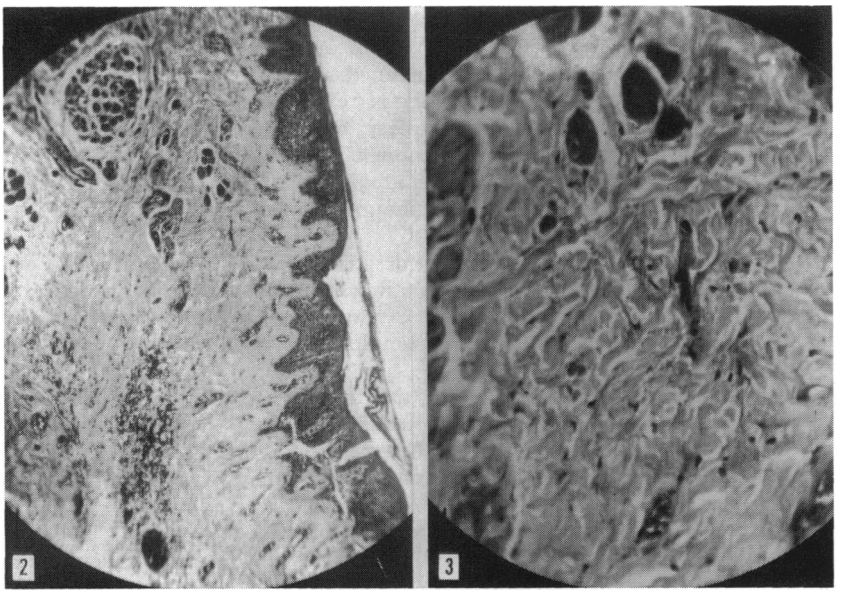

FIGURE 2. CASE 1

Photomicrograph showing broadening of conjunctiva, hyperkeratosis, and absence of tarsal plates and meibomian glands. Muscle of Riolan is included. Hemorrhage into connective tissue occurred at operation.

FIGURE 3. CASE 1

Photomicrograph showing replacement of tarsal plate by connective tissue. Note fibers of muscle of Riolan.

The palpebral conjunctiva of both lower lids was congested. Some ciliary injection was present in both eyes. Corneal nebulas were present in the lower quarter of the right eye and the lower third of the left eye; a few small, superficial corneal ulcers were seen in these areas.

Chlortetracycline (Aureomycin) ointment was used until operation, which was performed on the left eye April 17, 1953, by the Kuhnt-Szymanowski technique, as follows: The entire margin of the lower lid was split just posterior to the line of lashes. Since absence of the normal, firm structure of the tarsus made it impossible to remove a triangular wedge, apex downward, as the Kuhnt technique requires, the procedure was altered, and a wedge of tissue was removed from the middle of the lid, including the conjunctiva, connective tissue, orbicularis muscle, and skin. Then a triangular portion of skin, with the base directed upward and outward, was removed at the outer canthus, according to the Szymanowski technique. The triangular wound was closed with three interrupted sutures of 6–0 silk in the conjunctival aspect, with a single additional suture at the lid margin. The anterior flap of the split lower lid was undermined, moved temporally, and sutured to the upper and tempo-

ral aspects of the triangle with interrupted 4–0 and 6–0 silk sutures. Before the sutures were tied, the lashes now in the upper border of the triangular area were removed and this area was scraped.

At the conclusion of the operation the ectropion seemed, if anything, to be overcorrected. Twelve days later, however, after the sutures and bandages were removed, it began to reappear, though in considerably less pronounced form. The scar in the outer canthus gradually widened, eventually assuming the appearance of a flat keloid. The disappointing result was thought to be due to the absence of the tarsus.

On July 16, 1954, the procedure just described was repeated on the left eye and was also performed on the right eye, in which the tarsus, as in the left eye, was missing. The final result in the left eye was excellent. In the right eye, the result was poor, but the ectropion was completely corrected after the operation was repeated on July 22, 1955.

The patient is well satisfied with the improvement in her appearance (Figure 3). Photophobia is no longer troublesome and the keratitis has disappeared, but corneal nebulas are still present.

The pathologist reported as follows on the tissue removed at the first operation on the left eye:

This wedge-shaped piece of tissue fixed in Formalin measures 1.1 by 0.6 by 0.4 cm. One of its broad surfaces is covered by a brown, smooth membrane, which could represent skin and which continues over an acute border and upward on the opposite side, where it becomes white and resembles a mucosal lining. When the specimen is sectioned perpendicularly to these two surfaces, grayish white tissue without distinct layering is exposed.

Microscopic examination shows that the palpebral conjunctiva, which has undergone slight broadening, contains practically no mucus-secreting cells and shows slight hyperkeratosis (Figure 4). Beneath it is connective tissue, which is slightly hypervascularized. No tarsal plate is evident, and there is a total absence of meibomian glands. The connective tissue shows elastic fibers and well developed collagen (Figure 5).

Case 2 (II, 3; Figure 6). This forty-seven-year-old male, father of the propositus, was first seen on March 2, 1954, with the chief complaint of inflammation of both eyes due to inturned eyelashes. The condition had been present since childhood, and periodic epilation was carried out by a relative. The patient's vision had been poor in early childhood, and he had been operated on for congenital cataracts at the age of ten years.

Examination revealed the eyelids normal in position, with no ectropion or entropion, and of normal thickness. Palpation revealed the tarsus to be present. Although many lashes were missing in the upper lids, each lid had the normal anterior row of lashes. The usual openings of the meibomian glands were not demonstrable in either the upper or the lower lids. The posterior border of the margin of the right lower eyelid was ill defined and rounded; close to this border ten rather thin and short eyelashes were present in the nasal half and eight in the temporal half. These lashes lay chiefly along the margin of the lid, but some drooped forward and their shafts intermingled with the shafts of the anterior rows of lashes. Similar findings were demonstrable in the left lower lid, on which only twelve abnormal lashes were observed.

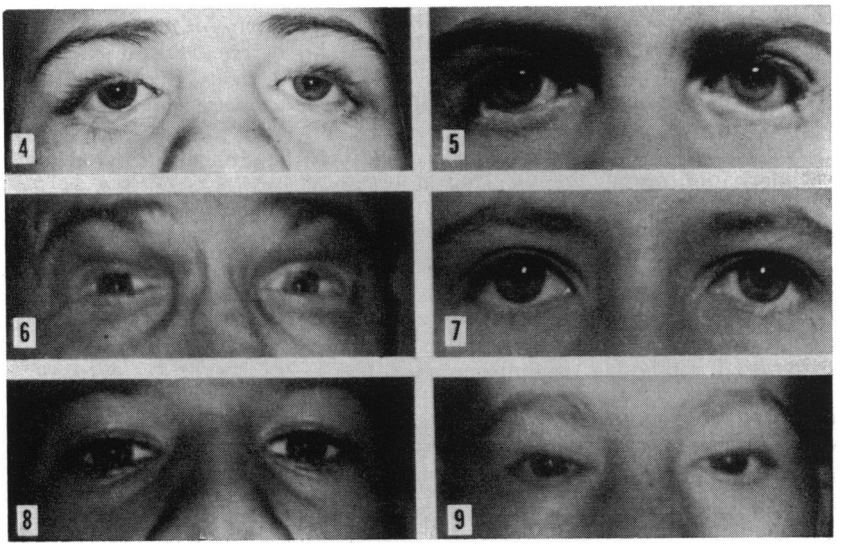

FIGURE 4. CASE 1

Ectropion of lower lids before operation.

FIGURE 5. CASE 1

Appearance of patient after surgical correction of ectropion.

FIGURE 6. CASE 2

Unnoticeable distichiasis is present; no ectropion.

FIGURE 7. CASE 3

Unnoticeable distichiasis is present; no ectropion.

FIGURE 8. CASE 4

Normal eyelids

FIGURE 9. CASE 5

Slight ectropion of lower lids; unnoticeable distichiasis is present in upper lids.

The twelve to fifteen additional lashes present in each of the upper lids arose close to the inner border of the lid margin, in the normal location of the meibomian orifices. Eight to ten of these aberrant lashes were in the temporal half of the lid and four to six in the nasal half. Some of them were of the lanugo type and were so pale, thin, and small that they could be seen only with the loupe or the slit lamp. Most of them were turned inward and rubbed against the eyeball, explaining the discomfort and irritation of the bulbar conjunctiva of which the patient complained.

The palpebral fissure was unusually narrow horizontally, measuring only 20 mm.; the finding suggested blepharophimosis. Measurements of the upper

eyelids by Fuchs's technique were as follows: right lid: height, 17 mm., vertical extension 25 mm., coefficient 1.47; left lid: height, 19 mm., vertical extension, 27 mm., coefficient 1.44. Although the coefficient was below the normal level in both upper eyelids, the lids could be completely closed and no lagophthalmos was present.

The cornea was clear, but examination with the slit lamp showed some vascularization for 2–3 mm. next to the limbus.

The patient was aphakic, and only small remnants of the lens capsule could be seen in each eye behind the iris.

Electrolytic epilation of the eyelashes arising from the posterior border of the margin of the upper eyelids was done with some difficulty; even with magnification, some of the lashes were difficult to demonstrate. Three epilations were necessary to eliminate them all and to relieve the discomfort and irritation of the bulbar conjunctiva.

CASE 3 (III, 6; Figure 7). The twenty-three-year-old sister of the propositus, who was examined on February 10, 1956, denied all complaints referable to her eyes except that they tired easily. On further questioning, she stated that her lashes had turned in since childhood.

Examination showed all lids normal in position. Palpation revealed normal tarsal plates in the upper lids and normal openings of the meibomian glands close to the posterior border of the lid margins. In the lower lids, which were abnormally thin, the tarsal plates were either absent or extremely deficient in thickness, and no openings of the meibomian glands could be demonstrated.

On each of the upper lids there was a normal row of eyelashes along the anterior border of the margin. On each of the lower lids there was also a normal anterior row of lashes, though they were rather short and pale. Near the posterior border of each lower lid was a row of fifteen aberrant lashes, all of them short, whitish, and thin. In the right lid, these lashes occupied only the nasal two thirds; in the left lid they extended almost to the outer canthus. All aberrant lashes were inclined along the border of the lid, except for three on each side in the region of the lacrimal punctum; here they turned inward and brushed against the bulbar conjunctiva, though not enough to produce inflammation.

CASE 4 (III, 7; Figure 8). The fifteen-year-old brother of the propositus was examined in July, 1956. He had been committed to a government institution for children, in which he was classified as a moron.

Examination showed the eyes to be normal in all respects. The eyelids were also normal in position, thickness, structure, tarsal plates, eyelashes, and openings of the meibomian glands.

The palpebral fissures measured 28 mm. horizontally and 10 mm. vertically. Measurements of the upper eyelids by Fuchs's technique were the same on both sides: height, 22 mm.; vertical extension, 28 mm. The coefficient, 1.3, was below the normal of 1.5 set by Fuchs, but this boy did not have lagophthalmos and both lids were completely closed when he was asleep.

CASE 5 (III, 8, Figure 9). This fourteen-year-old girl, an illegitimate daughter of the father of the propositus, was examined on April 2, 1956. Although her

only complaint was photophobia, her mother stated that her eyelids were not completely closed when she was asleep.

Examination revealed slight ectropion of both lower lids, with a possible bilateral weakness of the orbicularis muscle. The lower lids were abnormally thin, and no tarsal plates could be felt on palpation.

The normal openings of the meibomian glands could not be demonstrated in either upper or lower eyelids. No aberrant lashes were present in the lower lids. The upper eyelids were normal in position and thickness, and the tarsal plates were apparently normal. On each upper lid there was the usual row of lashes, but a second row, of about fifteen lashes, was present in the temporal third. These aberrant lashes, which were smaller, paler, and thinner than those of the anterior row, arose from the posterior border of the lid margins where the openings of the meibomian glands are usually situated; no openings were seen elsewhere along the margin of the upper lids. The direction of the aberrant lashes was the same as that of the anterior rows of lashes, and they did not touch the eyeball when the lids were opened or closed. The eyelids did not close completely when the child was told to pretend that she was going to sleep.

The palpebral fissures were narrow, measuring 22 mm. horizontally on the right and 23.5 mm. on the left. The vertical measurement was 8 mm. on each side. Measurements of the upper lids by Fuchs's technique were the same on each side: height, 18 mm.; vertical extension, 24 mm.; coefficient, 1.33. The coefficient was below the normal of 1.5.

There was some congestion of the bulbar conjunctiva in each eye and slight ciliary injection inferiorly on the right side. Some opacities were present in the lower third of each cornea. Photophobia was extreme.

The conjunctivitis in both eyes, the keratitis on the right side, and the corneal opacities on the left side were considered due to the slight ectropion rather than to the distichiasis. Therefore, after treatment of the active keratitis in the right eye with an ointment containing tetracycline and hydrocortisone, a Kuhnt-Szymanowski operation was performed on the right lower lid on June 1, 1956. As in Case 1, no tarsal plate was found. The wedge of tissue removed from the middle of the lid included all tissues from the palpebral conjunctiva up to the skin in that area; the skin was not removed, as it had been in Case 1.

The pathologist reported as follows on the specimen:

This wedge-shaped piece of tissue, fixed in Formalin, measures 0.6 by 0.5 by 0.3 cm. One side, which is covered by conjunctiva, is white, smooth and glistening. The opposite side, which is the apex of the wedge, is brown and slightly uneven. On section, there is no layering evident, and the predominant coloration is gray.

On microscopic examination, the epithelial layer of the conjunctiva is seen to be very slightly broadened. It contains a few mucus-secreting cells. A slight infiltration with plasma cells, lymphocytes, and a few large mononuclear cells is observed immediately beneath the epithelium. The subconjunctival layer of fibrous tissue is broader than in the other case studied histologically (Case 1) and is likewise totally devoid of meibomian glands (Figure 10). The subconjunctival connective tissue is denser in some areas than in the other specimen; it contains numerous broad collagen bundles, as well as elastic fibers, but be-

neath the conjunctiva the tissue is loose and edematous (Figure 10). The root of a hair follicle, implanted in the deepest part of the orbicularis muscle, can be seen near the lid margin.

Results of surgery were good in this case. The right lower lid was better approximated to the eyeball, and the right eye was well closed when the child was asleep. The same procedure will shortly be carried out on the left side.

CASE 6 (II, 1; Figure 11). This fifty-six-year-old lawyer, paternal uncle of the propositus, complained of burning of the eyes and photophobia when he was examined on August 2, 1956.

Both upper eyelids were normal in position, but a definite ectropion was present in both lower lids. All four lids were much thinner than normal. No tarsal plates could be demonstrated in the lower lids, and the plates palpated in both upper lids were thin and small. Even with the slit lamp it was not possible to demonstrate openings of the meibomian glands in either upper or lower lids. A group of four or five lashes arose from the posterior border of the margin of each upper lid, about 1–2 mm. above the outer canthus, and similar groups were present 2 mm. further superiorly. These aberrant lashes, which were similar in appearance to those in the normal anterior rows in the upper lids, were inturned and rubbed against the eyeballs.

Slit-lamp examination revealed about fifteen aberrant lashes in the lower lids, arising from the margin close to the posterior border, along which they were distributed. They were not inturned and did not brush against the eyeball when the lids were closed.

The lids were apparently closed normally when the patient was asleep.

The palpebral fissures measured 24 mm. horizontally and 7 mm. vertically. In this patient, as in several other members of the same family, the small fissures, especially the short horizontal measurements, gave the impression of small eyes. Measurements of the upper lids by Fuchs's technique showed the height of each lid to be 17 mm. and the vertical extension 26 mm. The coefficient, 1.53, was low for the patient's age.

There was some congestion of the bulbar conjunctiva in both eyes, and a small corneal nebula was present in the left eye, next to the lower limbus.

Electrolysis of the inturned eyelashes has been recommended but has not yet been accepted.

CASE 7 (III, 1; Figure 12). This twenty-six-year-old dental student, a cousin of the propositus, was examined on August 2, 1956. His chief complaint was inturned eyelashes, with irritation of the eyeballs. Electrolysis of some of the lashes in the nasal third of both upper eyelids about a year earlier had not been successful; most of them had soon reappeared.

Examination showed very slight ectropion in the temporal half of each lower lid. All four lids seemed much thinner than normal. In the upper lids, undeveloped tarsal plates could be palpated about 4 mm. upward from the border, but no definite tarsal structures could be demonstrated in either lower lid.

All four lids presented the normal anterior row of lashes. In the nasal half of each upper lid were fifteen aberrant lashes, which arose from the posterior border of the lid margin. They were somewhat thinner and shorter than the

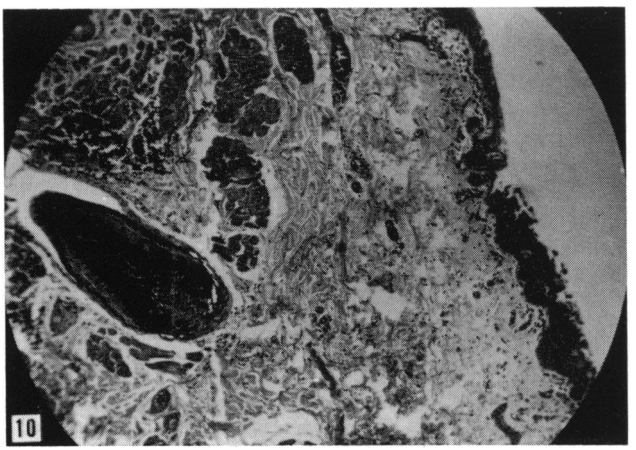

FIGURE 10. CASE 5

Photomicrograph showing replacement of tarsal structures by lax fibrous tissue; no meibomian glands are present.

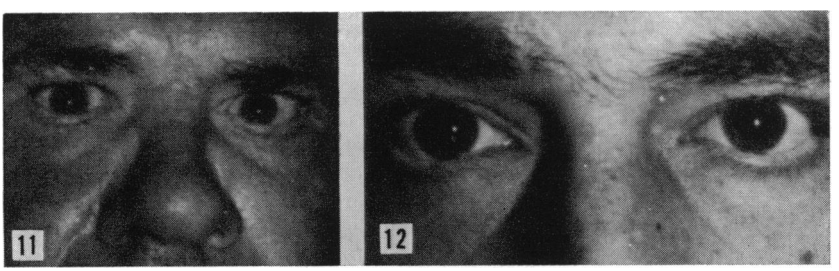

FIGURE 11. CASE 6

Slight ectropion of lower lids. Small palpebral fissures give impression of "small" eyes. Unnoticeable distichiasis is present in upper and lower lids.

FIGURE 12. CASE 7

Slight ectropion of lower lids; distichiasis present in all four lids, but noticeable only in nasal third of each upper lid.

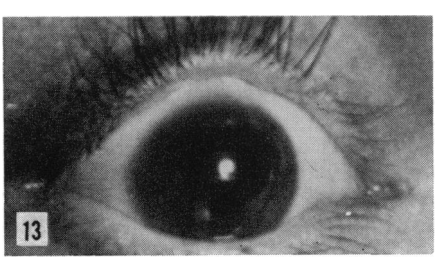

FIGURE 13. CASE 7

Slight ectropion of right lower lid; distichiasis present in upper lid.

normally placed lashes and the shafts of most of them rubbed against the eyeball. There were three additional aberrant lashes in the right upper lid, close to the outer canthus (Figure 13), and eight similarly placed aberrant lashes in the left upper lid. In the nasal half of each lower eyelid ten or twelve small, white, lanugo-like hairs arose from the posterior border of the lid margin; they were inclined along the lid margin and therefore did not rub against the eyeball. The normal openings of the meibomian glands could not be demonstrated in any of the eyelids. The patient closed his lids well while he was asleep.

Measurements of the upper lids according to Fuchs's technique showed the height of each lid to be 22 mm. and the vertical extension to be 30 mm. The coefficient was 1.36.

The bulbar conjunctiva was slightly injected. There were no corneal opacities.

Electrolytic epilation of the aberrant inturned lashes in the upper lids was done on August 7, 1956, with excellent results.

CASE 8 (IV, 1; Figure 14). This four-year-old second cousin of the propositus was examined on August 2, 1956. She had no complaints referable to her eyes, and all findings (lids, lashes, openings of the meibomian glands) were entirely normal. Measurements of the upper lids by Fuchs's technique showed the height to be 18 mm. and the vertical extension 26 mm. The coefficient, 1.45, was slightly below the established normal.

CASE 9 (IV, 2; Figure 15). This two-year-old boy, a second cousin of the propositus, was examined on August 2, 1956. According to his parents, ectropion had been present in all four eyelids since birth, and the eyelids did not close completely when he was asleep.

Examination showed marked ectropion in all four lids, most evident and most complete in the lower lids, in which the palpebral conjunctiva was completely exposed. In the upper lids, the anomaly was only partial when the eyes were open but became complete when they were closed (Figure 16). Tarsal plates could not be demonstrated in any of the four lids.

On the upper lids the growth of eyelashes was entirely normal. On the lower lids the normal, anteriorly placed lashes were thin and pale, and on each side some fifteen or twenty lanugo-like hairs arose from the posterior border of the margin. Some of these aberrant lashes were turned inward and rubbed against the eyeball. Normal openings of the meibomian glands were not present in any of the lids.

The palpebral fissures measured 22 mm. horizontally and 8 mm. vertically. The upper eyelids were definitely shorter than normal. By Fuchs's technique the height was 17 mm. and the vertical extension 20 mm., which gave a coefficient of 1.12.

The palpebral and bulbar conjunctiva was congested. Some opacities were present in the lower quarter of each cornea.

Plastic surgery has been recommended to this patient. The abnormal shortness of the eyelids will require tarsorrhaphy, with skin grafts applied to all four lids.

CASE 10 (III, 2). This twenty-four-year-old cousin of the propositus was not available for personal examination, but Dr. Edmund B. Spaeth has informed

me that he operated on him, when he was twenty-one years of age, for congenital ectropion of all four lids, which had been evident since birth. He had a superficial punctate keratitis as the result of incomplete closure of the lids and exposure of the cornea. A severe chronic photophobia made it impossible to secure photographs. The ectropion was corrected with skin grafts, without resection of any tissue, with excellent results. No information is available in this case concerning the condition of the tarsus or the presence or absence of distichiasis.

CASE 11 (III, 3; Figure 17). The ten-year-old female cousin of the propositus was examined in May, 1956. No abnormalities of any kind were evident. Measurements of the height and vertical extension of the upper eyelids were not secured.

CASE 12 (III, 4). The seven-year-old male cousin of the propositus was examined in May, 1956. All findings were normal. Measurements of the height and vertical extension of the upper eyelids were omitted. Because of the child's lack of cooperation, photographs could not be secured.

CASE 13 (III, 9). The sixteen-year-old cousin of the propositus was not available for personal examination, and information concerning him was secured from Dr. Edmund B. Spaeth, who operated on him at the age of fifteen years, for ectropion which had been present since birth and which affected all four lids. The boy had a superficial punctate keratitis, due to incomplete lid closure, and a chronic severe photophobia, which made it impossible to secure photographs. The ectropion was corrected with skin grafts, without resection of any tissue, with excellent results. No information is available concerning the condition of the tarsal plates or the presence or absence of distichiasis.

CASE 14 (II, 5; Figure 18). This forty-four-year-old lawyer, uncle of the propositus, was examined in May, 1956. He complained of some irritation in the right eye and considerable photophobia. He had had slight ectropion of both lower lids since birth, and had a history of inflammation in the left eye in infancy and again in 1938 and 1946.

Examination revealed slight ectropion of both lower lids, more pronounced in upper gaze. No tarsi were demonstrable in the lower lids. In the upper lids the tarsal plates were slightly thinner than normal and extended less far upward than normal.

In addition to the usual anterior row of lashes present in the upper lids, a bunch of eight lashes arose from the posterior border of the lid margin, 2 mm. from the outer canthus. They were inclined toward the eyeball and sometimes rubbed against it (Figure 19). The anterior lashes on the lower lids were whitish and weak-looking and were far fewer than the number usually present. In the middle third of each of the lower lids were some almost invisible, lanugo-like lashes which arose from the lid margin, close to the posterior border. The normal openings of the meibomian glands could not be demonstrated in any of the four eyelids.

The palpebral fissures were narrow in the horizontal diameter, measuring only 24 mm. on each side. Vertically, the lids opened 10 mm.

There was some congestion of the bulbar conjunctiva in each eye. In the right eye a faint corneal nebula extended upward from the limbus for 3.5 mm.

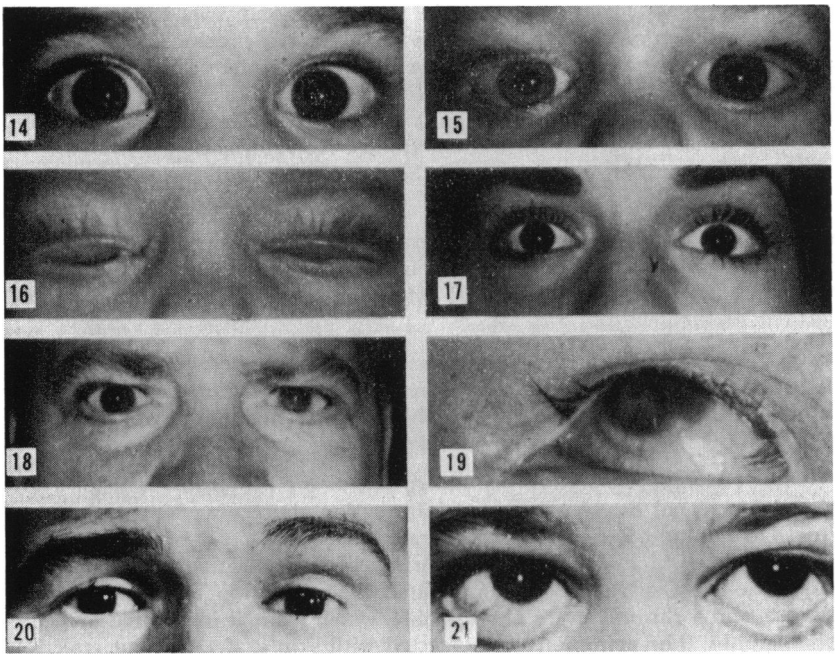

FIGURE 14. CASE 8

Normal eyelids.

FIGURE 15. CASE 9

Ectropion of some degree in all four lids; distichiasis present in lower lids but not seen because aberrant lashes are pale and thin.

FIGURE 16. CASE 9

Ectropion of upper lids when lids are closed.

FIGURE 17. CASE 11

Normal eyelids.

FIGURE 18. CASE 14

Slight ectropion of lower lids; distichiasis present in all four lids but noticeable only in upper lids close to outer canthus.

FIGURE 19. CASE 14

Left eye; distichiasis in upper lid near outer canthus; dense vascularized corneal macula.

FIGURE 20. CASE 15

Slight ectropion of lower lids; unnoticeable distichiasis present in all four lids.

FIGURE 21. CASE 16

Ectropion of all four lids before surgical correction.

In the left eye the nebula, which occupied the lower two thirds of the cornea, was denser than on the right and superficial vascularization was present.

CASE 15 (III, 10; Figure 20). This fourteen-year-old cousin of the propositus was examined in New York on July 6, 1956, through the courtesy of Dr. Ramón Castroviejo, who also made available to me the previous medical record. The boy had a history of irritation of both eyes in early childhood but had no complaints at the time of the 1956 examination.

A very slight ectropion was present in both lower lids, in neither of which was a tarsal plate demonstrable. In the upper lids there was no evidence of a tarsal structure in either the nasal or temporal third, and only a very small plate in the middle third.

The normal anterior row of eyelashes was present in all four lids. On the right upper lid four aberrant lashes arose from the posterior border of the margin, about 1 cm. from the outer canthus, and a single lash, of similar origin, was present about 5 mm. from the inner canthus. There were no aberrant lashes on the right lower lid. On the left upper lid there was an aberrant row of about forty lashes, similar in color, length, and direction to the normal anterior row. They arose from the posterior border of the lid margin and were localized in the middle three fifths of the border. On the left lower lid a single pale, thin lash arose from the posterior border of the lid margin, in the middle third. None of the aberrant lashes brushed against the eyeball. Normal openings of the meibomian glands were not observed in any of the four lids.

The margin of the left upper eyelid was normally placed except when the patient looked upward; then a slight entropion was evident, but even under these circumstances, the extra row of eyelashes, though they were in close approximation to it, did not rub against the eyeball.

The palpebral fissures were narrow in the horizontal diameter.

CASE 16 (III, 11; Figure 21). This twelve-year-old female cousin of the propositus was examined in New York on July 6, 1956, through the courtesy of Dr. Ramón Castroviejo, who also made the clinical records available. Dr. Castroviejo first saw the patient in October, 1947, when she was three years old. She had a history of ectropion of all four eyelids since birth and slept with the eyes partly opened. Examination at this age showed slight ectropion of both upper lids and more pronounced ectropion of both lower lids. Although the patient did not cooperate in the examination, it was evident that she had some inturned lashes and that corneal nebulas were present in each eye.

Surgical correction of the ectropion by skin grafting was carried out on both right eyelids on September 2, 1948, and on both left eyelids on November 4, 1948. The immediate results were good, and when the child was examined in July, 1956, the ectropion was completely corrected, the cosmetic results were excellent, and the lids closed satisfactorily.

Examination at this time showed six aberrant lashes on the upper right lid, arising from the posterior border of the margin at the junction of the nasal and middle third. Four aberrant lashes were similarly located in the lower right lid. These lashes rubbed the eyeball when the patient looked down and to the left. On the left side, one inturned lash arose from the posterior border

of the margin of the upper lid near the outer canthus, and another arose in the lower lid in the same position. Both of these lashes, especially the lower, rubbed against the eyeball. The aberrant lashes were all dark but seemed weaker and thinner than the lashes in the normal anterior rows.

The palpebral fissures measured 25 mm. horizontally and 12 mm. vertically in the right eye, with maximum effort. In the left eye the corresponding measurements were 24 mm. and 12 mm.

The patient had a dense, vascularized nebula in the lower third of each cornea. She had considerable photophobia.

REVIEW OF THE LITERATURE

ECTROPION

The twelve case reports which make up the literature on congenital ectropion can be divided into two groups. The first group (group 1 of the proposed etiologic classification) consists of only five cases. The other seven cases, including the first case reported, by Adams (6) in 1896, are instances of group 2 of the proposed classification.

Group 1. The first case of congenital ectropion of the eyelids was reported by Urmetzer (7) in 1914, at a meeting of the Vienna Ophthalmological Society and was mentioned by Landau (8) in his 1947 contribution. The patient, whose age and sex are not mentioned in the abstract available to me, also presented abnormal shortness of the affected lower lids, severe redness of the lid margins, and madarosis. Complete closure of the lids was not possible. When the patient was asleep, the palpebral fissure remained open for a space of 3 mm. The lids were scarcely longer on stretch than when they were relaxed. Treatment consisted of the application of ointment and a bandage during the night; the results were not stated.

In 1915, Treacher Collins (9) reported congenital ectropion of the lower eyelids, present since birth, in a four-months-old child. Examination also revealed well marked epicanthus and partial ptosis of the lids, which appeared too large to fit the eyeballs closely. There was no family history of congenital defects of the eyes or eyelids.

Operation was done when the child was four years and ten months old; during the interval there had been no change in the anomaly. A wedge-shaped piece of tissue was resected through the whole thickness of the right lower lid, just internal to the outer canthus. Microscopic examination of the specimen showed the orbicularis to be well developed and the group of fibers near the free border of the lid (the muscle of Riolan) to be exceptionally numerous. The epithelium of the palpebral conjunctiva was several layers thick, and there was some

papillae formation, apparently the result of exposure. There was no description of the tarsus.

In 1944 Gordon and Cragg (10) reported an instance of congenital ectropion, associated with bilateral ptosis, in a twenty-three-year-old white man, who complained of ocular discomfort because of the deformity. He also suffered from mild epiphora. He slept with his eyes open, and a mucoid discharge accumulated in the palpebral fissures during the night. Dust and dirt produced so much irritation that he could work only in selected enviroments.

The palpebral fissures sloped slightly downward and outward. Mild ectropion was present in the outer half of all four lids, especially the lower lids. The upper lids were abnormally short and could not be elevated actively. The lashes were normal in position and distribution.

Treatment consisted of skin grafting followed, four months later, by the creation of fascial slings to secure the upper lids to the frontalis muscles and thus overcome the ptosis. The tarsus was not described in the notes on examination or operation.

The patient had no personal recollection of his father but had been told that he had suffered from a similar deformity of the eyelids. Two of the patient's six brothers and one of his three sisters also had similar defects, though less marked than his own. The mother's eyes were normal.

The cases reported by Landau (8) and Erdmann (11) are described under the heading of distichiasis, since the anomaly of the lashes was more pronounced in them than was the ectropion.

Group 2. The first recorded case of congenital eversion of the eyelids, reported by Adams (6) in 1896, concerned a two-months-old child who was born with both upper lids completely everted and greatly swollen. The palpebral conjunctiva was markedly thickened at the time of the examination. When the lids were placed in the normal position, they remained in it only while pressure was maintained. The use of compresses restored the lids to a permanently normal position in about a month.

In 1909, Erb (12) reported congenital ectropion of both upper eyelids in a two-day-old child, born after a prolonged labor due to breech presentation. The everted upper eyelids, which were large and edematous, were covered with bluish-red mucosa, which in turn was partly covered with scabs. Active bleeding followed the removal of the scabs. The lids were replaced without difficulty after the child was anesthetized. They were held in position by adhesive tape. When it was removed five days later, they were in their normal position and the eyes

opened well, but the upper eyelids were still larger than normal and were atonic.

In 1920, Mertens (13) reported congenital ectropion of both upper eyelids in a two-day-old child, born after a long and difficult labor due to a contracted pelvis. The upper eyelids were completely everted and the conjunctiva, which was enormously swollen, was puffy and red. Treatment consisted of the application of boric acid and vaseline.

The child was well developed and was apparently normal immediately after birth, but death occurred at four months from hydrocephalus and convulsions. The physician in charge of the case reported that the ectropion had been relieved, but that the palpebral fissures were narrowed, especially at the inner canthus, and were oblique from the upper outer toward the lower inner angles.

In 1954, Young (14) reported congenital ectropion of the upper eyelids in a newborn infant weighing 7 pounds 12 ounces and born after an easy six-hour labor. The pregnancy had been entirely normal except for a mild pre-eclamptic toxemia in the seventh month. Five previous pregnancies had resulted in normal children. The sixth (immediately preceding) pregnancy had terminated in a stillborn child with hydrocephalus and congenital meningocele.

During the labor in question, as soon as the head appeared at the outlet, it was observed that both upper eyelids were completely everted and that their entire inner surfaces, together with a large part of each upper transitional fold, were exposed. The transitional folds were so swollen that the lid openings were completely obliterated. The ectropion appeared as large edematous swellings covered by bluish-red mucosa; when the child cried, the swelling increased and the coloration became more distinctly bluish. The lower lids appeared normal, but the eyes, which were observed only with great difficulty after retraction of the lower lids, seemed smaller than normal. The infant had the characteristic stigmata of mongolism.

On the eighth day of life, under general anesthesia, the excess tissue beneath the right upper eyelid was excised and the raw conjunctival margins were united by a continuous suture. The child died suddenly the following day, after an attack of cyanosis. Death was apparently unrelated to the operation.

Complete histologic examination of both upper lids at autopsy showed no intrinsic defects. A marked overdevelopment of the epicanthic fold was demonstrated on the outer surface of each upper eyelid, in the region of the inner canthus. Section of the eyeballs revealed all the intraocular tissues to be normal in structure and position.

In 1954, Ostriker and Lasky (4) reported a case of congenital ectropion, which, they stated, had no previous parallel in the literature, though the description and photographs suggest that this case closely resembles the cases reported by Erb (12), Mertens (13) and Young (14), which have just been summarized. In Ostriker and Lasky's case, a newborn child, born after a short, spontaneously terminated labor, showed "thickened, swollen, injected, totally everted upper eyelids," without other associated ocular or general anomalies. By the third week of life the eyelids had become normal and so remained.

In 1955, Hopen (15) reported a case of complete congenital eversion of the upper eyelids in a full-term Negro boy, born after a labor which was uneventful except for a slight arrest of the head on the perineum. The mother, a fourteen-year-old primigravida, was RH positive.

The upper eyelids were markedly chemotic, thickened, and edematous and were totally everted. The condition was not improved by the continuous use of saline compresses, chlortetracycline (Aureomycin) ointment and adhesive straps. On the fifth day of life, under light ether anesthesia, the lids on both sides were sutured together in the outer, middle, and inner aspects of the margins with three mattress sutures of black silk applied over small rubber dams. Two days later, when the sutures were removed, the lids were in normal position, and apposition was satisfactory, even when the child cried. Improvement was permanent.

In 1955 Mazhar (16) reported congenital eversion of the upper eyelids in a seven-day-old Arab child, born at full term. The eversion, which was associated with chemosis and edema, had been present since birth. There was a moderate amount of secretion. Treatment by warm saline compresses and oxytetracycline (Terramycin) ointment restored the lids to normal position and condition within 2 weeks, so promptly, in fact, that the author wondered whether he had really been dealing with a true developmental anomaly.

DISTICHIASIS

Distichiasis, a term derived from the Greek words meaning double and row, indicates the presence of an aberrant posterior row of eyelashes which emerge from the sites of the normal openings of the meibomian glands. The term was suggested by Fuchs (5) in 1889. Erdmann (11), in 1904, championed the term distichiasis for the true congenital condition. At that time the terms trichiasis and distichiasis were still being used rather loosely, to indicate any sort of abnormal position of the eyelashes. DeVoe and Horwich (17) employed the term tetrasti-

chiasis, apparently because in their case there were four rows of lashes, two normal and two aberrant, on the affected lids.

Distichiasis, which is a congenital condition, must be differentiated from the acquired abnormal condition known as trichiasis, a word which indicates malposition and maldirection of the lashes. Fuchs considered the noncongenital forms of distichiasis, such as occur in trauma, as basically the same as trichiasis, from which they differ only in degree.

The first report in the literature on congenital distichiasis, by Becker (18) in 1867, consisted of two cases. The original article is not available to me, and I quote from Kuhnt's summary of the cases.

The first patient, an eight-year-old girl, had suffered from disorders of the eyes for six years. The cause of the severe spasm of the lid was found to be a second row of cilia on the inner side of the lid margin, immediately adjacent to the orifices of the meibomian glands. These cilia were light blond and so regular in arrangement, length and direction that when the lid was lifted from the eyeball, they looked like the teeth of a fine comb. When the lid lay upon the eyeball, the lashes adapted their form to its convexity; they brushed against the conjunctiva and cornea upon up and down movement, but without injury to them. The intermarginal portion of the outer border of the lids was wider than normal but had the peculiar shine of normal lids. In this area were a number of individual, extremely fine, scarcely visible small hairs.

Becker's second patient, a thirteen-year-old girl, suffered from catarrhal conjunctivitis. The only abnormality evident on examination was a second row of cilia on both lower lids, close to the openings of the meibomian glands. These lashes turned inward and irritated the eyeball.

In 1880, Nicati (19) reported a patient with photophobia and conjunctivitis caused by distichiasis. When he excised a piece of the lid margin, microscopic examination showed the points of implantation of the abnormal cilia, which were readily recognizable as they emerged from the inner edge of the lid margin, opposite the outer row of cilia. There was no doubt that these aberrant cilia emerged from the openings of the meibomian glands. Between the normal and anomalous rows of cilia the lid margin was entirely normal.

In 1891, Herrnheiser (20) reported a case of distichiasis in a twelve-year-old boy who had suffered from red eyes throughout childhood. There was a double row of cilia on all four lids, the second rows taking the place of the normal orifices of the meibomian glands. The aberrant cilia were lighter in color than the normal lashes and resembled the

lanugo-like hair the patient had over his whole body. The aberrant lashes pointed upward or downward, depending upon their location, and brushed against the eyeball, apparently without harming it.

Examination of serial sections of a piece of tissue excised from the lid margin showed that each aberrant eyelash corresponded in location to a gland whose excretory duct opened into the hair follicle. The roots of the cilia lay almost entirely outside of the excised section. The glands opened, like sebaceous glands, into the upper half of the hair follicles but had the structure of meibomian glands. They terminated within the excised portion and apparently did not extend upward. The number of both cilia and glands corresponded to the normal number of meibomian glands. Microscopically, no true meibomian glands were found, and the glands which were present appeared very slightly developed and seemed to serve as appendages to the abnormal cilia.

In 1899, Wood (21) reported two cases of congenital distichiasis, in a father and a daughter. Each patient had an aberrant row of fine white hairs which emerged from the inner border of the lid margin and at times brushed the cornea. Hotz (22), in a discussion of this paper, mentioned a similar case, in which fine cilia were apparently implanted in the secretory ducts of the meibomian glands.

In 1899, Westhoff (23) reported distichiasis in an eight-year-old child who suffered from photophobia, left convergent strabismus, and reddening of the conjunctiva. On the sharp inner border of each eyelid were about fifteen aberrant lashes which were normal in appearance except for their unusual length. On the upper lids these lashes emerged only from the inner border. On the lower lids a few also emerged at some distance from the border. The orifices of the meibomian glands were visible in this case. This child's anomaly had existed since birth. A similar condition was present in her mother, her three-year-old brother, and her mother's brother. Two other siblings were normal.

In an extensive paper on distichiasis published in 1899, Kuhnt (24) described a fifty-two-year-old woman who had suffered from inflamed eyes and photophobia since childhood and who had required epilation for many years.

There was considerable blepharospasm and lacrimation on examination. The conjunctiva was slightly injected. On both corneas were dense and diffuse cicatricial opacities. Vision was limited to finger counting at 1 to 1.5 meters.

On each lid, in addition to the normal anterior rows of cilia, a row of fine, light, soft, lanugo-like lashes emerged directly from the intermarginal portion. These hairs, which were easily visible to the naked

eye, were turned toward the eyeball and brushed against the cornea with each movement. By means of a magnifying glass it was seen that the intervals between them were similar to the intervals between the orifices of normal meibomian glands. The orifices of the normal glands were, however, not demonstrable.

On microscopic examination of a full-thickness wedge of tissue from each lid, the prominent findings were: absence of the meibomian glands; their replacement by well developed cilia with all their characteristics; the presence of a double row of Krause's glands in the tarsus; and the presence of unusually well developed Moll's glands at the posterior row of pseudo-cilia. The tarsus seemed less firm than normal.

This patient suffered from elephantiasis of the calves, as did one of her daughters, but no further evidences of congenital anomalies in the family could be elicited.

In 1904, Erdmann (11) reported three cases of congenital distichiasis in three generations of a family. The grandmother, who was fifty-two years of age, stated that her parents and sisters had had "weak eyes," and that she herself had suffered from inflamed eyes and had required epilation since early childhood. There was slight photophobia in both eyes. The lid margins were moderately thickened. The lids were in normal position, though the two lower lacrimal puncta were slightly everted. The tarsal conjunctiva was red and swollen, and the palpebral conjunctiva was greatly injected. Both corneas showed considerable cloudiness and vascularization in the lower portions, and there was a small corneal ulcer on the left.

Examination with a magnifying glass showed rows of aberrant cilia on all four lids. These lashes, some of which were light and some pigmented, were soft, 3–5 mm. long, chiefly of the lanugo type, and without the thickness of the anterior cilia. They lay close to the rather sharp inner borders of the lid margins and parallel to them. They emerged from tiny, regularly arranged openings, which corresponded in number and position to the openings of the meibomian glands. Hairs appeared in the lower lids in all of these openings, in almost complete, regular rows, but many openings on the upper lids were without hairs. The aberrant lashes pointed upward or downward, depending upon their location. Sometimes they pointed backwards, the longer lashes touching the eyeballs with their entire surface and the shorter lashes touching them only with their points. The aberrant lashes brushed against both the cornea and the conjunctiva.

Histologic examination of sections excised from the lower lid showed moderate thickening of the tarsus, whose tissue was less firm and less

sharply delimited from the surrounding area than in a normal lid. In the tarsus, close to its transition into the tissue of the lid margin, were embedded glandular alveoli, which were scantier than normal meibomian glands but were quite similar to them in structure and position. These alveoli were connected with the hair follicles. The posterior cilia, which were quite rudimentary, were of small diameter. The papillae were small. The Moll's glands which were present opened into the hair follicles.

The daughter of this patient, who was twenty-one years of age, had had frequent inflammations of the eyes in childhood and what she described as occasional "strong flows" of tears later in life. She had distichiasis of all four lids, but the aberrant eyelashes were less numerous than those of her mother or her daughter. A large number of openings on the inner margin of the lids, which were assumed to be orifices of meibomian glands, were without lashes. The structure and position of the aberrant lashes were similar to these features in the mother's case.

This second patient's child, a six-year-old girl, had always had red eyes, associated with slight lacrimation. Examination showed irritation and photophobia. The tarsal conjunctiva was somewhat reddened and swollen and the conjunctiva of the eyeball was slightly injected. The cornea looked normal on superficial inspection, but on closer examination was found to have a slightly roughened surface and to be less shiny than usual, because of a slight irregularity of the epithelium.

On the inner border of the margin of all four lids, very fine, light, lanugo-type hairs, 6–8 mm. long, emerged from openings corresponding to those of the meibomian glands. These lashes, twenty-five to thirty in number on each lid, formed complete, perfectly regular rows. Although they turned slightly inward and brushed the cornea and conjunctiva with their entire surfaces, there was no evidence of any significant irritation.

Histologic study of a section from the right upper lid showed a few glandular acini which corresponded in all respects with meibomian glands except that they opened into well developed hair follicles of weak lashes instead of into a common excretory duct.

In 1906 Brailey (25) reported a case of a fourteen-year-old boy with a chronic conjunctivitis which had caused hyperemia and excoriation of the lid margins. The cornea showed delicate maculas. Numerous fine hairs were present in both upper and lower lids; they arose from the posterior margins, presented as single, closely placed rows, and were delicate and almost colorless. They were about half the length of the normal anterior cilia, from which they were separated by the full width

of the intermarginal space. These aberrant lashes lay upon the cornea. On examination with a lens, it was found that what had at first been assumed to be the orifices of the meibomian glands were actually follicles of the accessory cilia; the normal glands were not present. Microscopic study of a small specimen obtained from the center of the upper lid, including the conjunctiva and the entire thickness of the tarsus, showed no trace of the meibomian glands or of any epithelial cells. The tarsus was of normal thickness, density, and structure. Brailey considered that the section was too small to permit conclusions, adding that glands might have been present in other parts of the tarsus or in a rudimentary state near the lid margin, no portion of which was included in this specimen. This patient had two accessory bicuspid teeth, representing another possible instance of developmental error of the epithelial structures.

In 1912 Traquair (26) reported distichiasis in an eighteen-year-old boy who had suffered from irritation in the left eye for about a year. The lower lids were slightly shortened vertically and the skin over them seemed less loose than usual. There was a minimal degree of distichiasis in both lower lids. No meibomian glands could be demonstrated and it could not be determined whether the tarsal cartilage was present or absent. The condition was considered to constitute an almost complete absence of cilia and intermarginal zones.

Three other siblings were normal, but a similar anomaly was present in the patient's father, without obvious distichiasis. "Small and tender" eyes were characteristic of the paternal side of the family; the paternal grandmother and two other relatives on that side had "small" eyes. It seemed reasonable, according to Traquair, to explain the anomaly by the presence of an abnormality of the cilia.

In 1913, Begle (27) reported distichiasis in a thirty-year-old woman who had suffered from irritation of the right eye for a year; a year earlier she had had a corneal ulcer. The inner border of the margin of each lid presented a row of cilia, instead of the orifices of the meibomian glands. The aberrant cilia were black and 3–5 mm. long; because the angle of the margin was slightly rounded, they rubbed against the cornea lengthwise instead of with their tips. There were thirteen and seventeen accessory cilia, respectively, on the lower lids, and seven and eight, respectively, on the upper lids. A few glandular openings were observed on each lid in line with the accessory cilia. A mild degree of conjunctivitis was present, and there were several opacities and small corneal ulcers on the left eye.

Microscopic examination of strips of tissue from the lower lids,

which included the upper third to the upper half of the tarsi, revealed absence of the meibomian glands and their replacement by (1) hyperplastic sebaceous glands which discharged into the follicles of well developed accessory cilia and (2) small, simple, independent sebaceous glands scattered irregularly just beneath the lid margin and discharging upon its surface.

In 1923, Von Szily (28) reported distichiasis in a fifteen-year-old boy, who complained of severe photophobia. His parents and siblings presented no anomalies. Since birth, this boy had had a second row of cilia on the inner border of each lid margin; they apparently took the place of the openings of the meibomian glands. There were thirty-six hairs, all turned slightly inward, on the right upper lid; the few glandular orifices present were free of hair and were covered with secretion. All of the additional lashes brushed against the cornea and, when the eyes were closed, their points lay in the conjunctival sac. There were thirty aberrant cilia on the right lower lid, spaced at fairly regular intervals; they were finer and lighter than the normally located cilia, and their points turned inward. The twenty-four accessory cilia on the left upper lid were strongly developed and were only slightly lighter than the normally placed anterior row. They appeared less frequently in the nasal third than elsewhere. When the lids were open, these cilia were chiefly bent outward, but when the lids were closed, they were also within the palpebral fissure. The cilia on the temporal half of the lid, whose tips were bent, were entirely within the conjunctival sac. On the left lower lid, twenty-six aberrant lashes all emerged from the orifices of the meibomian glands. The conjunctiva of the lower lids was thickened and swollen. There were several opacities in the lower right cornea.

Examination of sections of the posterior portions of both upper lids and the left lower lid, removed through an intermarginal incision, showed the tarsus of normal firmness and almost normal length and width. The ciliary follicles and hair shafts were normal. The structure of the sebaceous glands was similar to that of meibomian glands, but these glands were too small to be meibomian glands and too strong to be ordinary hair follicles. Moll's glands were absent in some areas, particularly in the lower lid; elsewhere they were of various degrees of development.

In 1924, Blatt (29) reported five instances of congenital distichiasis in three generations of a single family, all of whom suffered from nervous diseases. The grandmother, who had had "seizures" in childhood, had two rows of cilia on each of the lower eyelids. Her son, who

had epilepsy, had two rows of cilia on all four lids. Her daughter, who also had epilepsy, presented the same anomaly. The elder son of the son, like his paternal grandmother, had two rows of cilia on the lower lids. His younger brother, then seventeen, was just beginning to complain of his eyes; he also had two rows of cilia on both lower lids. A daughter of the daughter, aged twelve, had no ocular complaints and presented no ocular abnormalities. Microscopic examination of the cilia in some of these cases showed structural abnormalities.

In 1927, Doherty (30) reported distichiasis in a seven-year-old boy, who had a second row of lashes arising from the inner margin of each lid. The accessory lashes were as numerous and as well developed as those of the normal anterior row. Although they rested against the cornea and the patient complained of lacrimation and of a feeling of sand in his eyes, no corneal opacities could be detected with the microscope. The aberrant lashes were removed by electrolytic epilation.

In 1927, Frolowa (31) presented the case of a fourteen-year-old boy who had suffered from lacrimation and photophobia since childhood. In place of the orifices of the meibomian glands he had twelve accessory lashes on the upper right lid, fifteen on the lower right lid, and fifteen and fourteen, respectively, on the left lids. Under the microscope, the aberrant cilia were lanugo-like, being shorter, thinner, and lighter than normal cilia. The medulla was either absent or scarcely noticeable. The shafts of the lower cilia brushed against the cornea, and when the eyes were closed the cilia rested on the conjunctival sac. In some areas in the accessory posterior row in which lashes were absent were small openings, at distances which corresponded to the openings of the meibomian glands. The corneas were transparent.

Microscopic examination of serial sections secured perpendicularly to the length of the tarsus showed that in some areas in the lower lid the acini of the meibomian glands were almost normal in number and size. In other areas the glands were rudimentary, particularly when there were hairs in the lumen; these glands were small, with two or three acini each, and suggested ordinary sebaceous glands. In some sections roots of the anterior row of normal cilia were seen next to the atypical lashes emerging from the meibomian glands. The roots of the anterior lashes were much thicker. Some sections from above the tarsal tissue showed a round, cyst-like formation, with clusters of fine rolled hair.

This patient's father presented the same anomaly, except that it was confined to the lower lids. Other members of the family, including the deceased mother, were reported to be without anomalies.

In 1935, Halbertsma (32) reported distichiasis in a thirty-seven-year-old man who had complained of photophobia, tearing, and blepharospasm, more troublesome on the left, since the age of eighteen. No family history of eye difficulties was secured. There were double rows of cilia on all four lids. The cilia of the posterior rows were less thick and were located vertically, at irregular distances. The posterior hairs numbered from ten to twenty on each row, and each row formed an angle of 90° with the normal anterior row. The aberrant lashes were from 2 to 3 mm. long. Their shafts touched the bulbar conjunctiva as well as the cornea, which presented numerous opacities, especially on the left. The bulbar and tarsal conjunctiva was red and swollen.

Histologic examination of an excised specimen showed part of the shaft of a pseudo-eyelash present in the orifice, which opened near the posterior border of the lid. The other end of the hair follicle formed the orifice of a glandular mass which appeared to originate from sebaceous glands and which consisted of some ten to twelve small lobes. These small lobes united to form larger lobes, one of which opened directly in the hair follicle. On both sides of the follicle were small glandular lobes which, in the section, were of the same structure as the glandular mass; they were regarded as possible outgrowths. A single small gland, a third of the way from the free border of the lid and quite close to the stem, had no opening. Apart from the acinous gland described there was no glandular tissue at the point of emergence of the shaft.

In 1938, Da Pozzo (33) reported two instances of congenital distichiasis, in a mother and one of her two sons. The woman had begun to complain of lacrimation, photophobia, and the sensation of a foreign object in the eyes at the age of twenty-seven, but her husband had been aware of the abnormal growth of her eyelashes for the preceding seven years. There were seven accessory lashes on the right upper lid, two on the left upper lid, and eight on the left lower lid. The posterior lashes, whose shafts brushed against the cornea, were shorter and less pigmented than the anterior lashes. All the hairs emerged from follicular orifices in the normal location of the orifices of the meibomian glands. Slit-lamp examination revealed orifices of meibomian glands from which no hairs emerged. The conjunctiva was reddened.

Histologic examination of two pieces of tissue from the left lower eyelid revealed both normal and rudimentary meibomian glands. The latter were similar in structure to normal glands but presented only two or three acini.

The five-year-old son of this woman presented the same condition as

the mother. The conjunctiva was not reddened and he did not complain of any discomfort.

In 1947, Landau (8) described distichiasis in a sixteen-year-old boy who, when his eyes were closed, presented a bilateral lagophthalmos of about 2.5 mm. The height of the upper lids by Fuchs's technique was 24 mm., the vertical extension 30 mm., and the coefficient 1.24. In both upper lids were rows of well developed accessory lashes. The cutaneous portion of the lid margin was slightly everted, particularly in the temporal portion. A fine dark line in the subtarsal sulcus, from which thin vertical streaks radiated, was thought to indicate the location of hair follicles of supernumerary cilia showing through the palpebral conjunctiva.

In 1949, Halberg and Paunessa (34) reported distichiasis associated with incomplete mandibulofacial dysostosis (Franceschetti's syndrome). There were double rows of lashes on all four lids, the accessory row on the upper lids being unusually long. Braley (35) reported a similar case in 1955, with severe corneal scarring.

In 1954 DeVoe and Horwich (17) reported congenital entropion and distichiasis (which they called tetrastichiasis) associated with palpebral hyperpigmentation and mental deficiency in a thirty-two-year-old Negro woman. An older sister stated that all these conditions had been present since birth. The sister also presented tetrastichiasis and trichiasis and had a vestigial accessory finger on the lateral margin of each hand. Another sister also had polydactyly.

The patient presented entropion of the lateral half of each upper eyelid for a distance of 13 to 14 mm. The palpebral fissures were 27 mm. long. Tetrastichiasis was present for the full length of both upper eyelids and trichiasis for the lateral half. There was one row of meibomian orifices in each eyelid. Irritation of the cornea by the accessory cilia had produced scarring of the lateral third on the right, and of the lateral half on the left. On eversion of the eyelids, which was achieved with considerable difficulty, the normal concavity of the tarsal plates was seen to be exaggerated laterally in the vertical meridian.

When a Streatfield-Snellen operation was done on the left upper lid, the tarsus was found completely normal except for the accentuated concavity. The cut surface of the slim wedge which was removed was also entirely normal.

COMMENT

THE LITERATURE OF CONGENITAL ECTROPION

Congenital ectropion caused by hyperkeratosis or ichthyosis congenita, as well as the variety caused by congenital microphthalmia or orbital cysts, presents no etiologic difficulties. The other varieties (Groups 1 and 2 of my proposed classification) are somewhat more difficult to analyze from this standpoint.

There are five recorded cases in the first group, congenital ectropion due to absence or anomalous development of the tarsus. In Urmetzer's (7) case the description available is too slight to warrant any discussion of the etiology. In Erdmann's (11) and Landau's (8) cases, the chief emphasis is on distichiasis, there being only casual mention of eversion of the eyelids. The descriptions of both Collins's (9) and Gordon and Cragg's (10) cases suggest that they are comparable to some of the cases in my own series, though in neither, unfortunately, is the report sufficiently detailed for a complete comparison.

Although Collins's report includes laboratory examination of an excised specimen from the affected eyelids, there is no mention in it of the state of the tarsus. His original idea, that the anomaly could be attributed to a developmental defect of the muscle of Riolan, whose function is to keep the border of the lids in contact with the eyeball, was not borne out by the findings; the muscle fibers, in fact, were unusually numerous. Collins's patient suffered from both ptosis and epicanthus, which were not evident in any of my series. Gordon and Cragg also do not describe the condition of the tarsus, although they could have examined it when skin grafts were applied to the lids. In their case the upper eyelids were short, as they were in Urmetzer's case and in several of my own cases. No abnormality of the lashes was found in either of these cases, in contrast to the distichiasis present with the ectropion in eight of my own cases.

The hereditary factor is not mentioned in Urmetzer's case. Collins specifically excluded it, though the possibility exists, of course, that the reported case was the first in the family and that the defect might become manifest in future generations. In Gordon and Cragg's case the hereditary factor was evident. The father apparently had the same condition, as did two of six brothers and one of three sisters, though it was less marked in the siblings than in the original patient. The type of heredity suggests dominance, but one cannot be definite, since the history covers only two generations.

In the ten living patients with ectropion in my series, the anomaly

involved all four lids in four cases (Cases 9, 10, 13, and 16) and was complete in the lower lids but less marked in the upper lids in all the cases. One other patient (Case 1) had complete ectropion of both lower lids, with normal upper lids. The five other patients (Cases 5, 6, 7, 14, and 15) had only slight ectropion of both lower eyelids. One patient (Case 15) also had a slight entropion of the left upper eyelid on upper gaze; the right upper lid was in normal position.

As already mentioned, no tarsus was found in two cases (Cases 1 and 5) on histologic examination of wedges of tissue removed from the lower lids; in Case 1 the ectropion was complete but in Case 5 it was only slight. These observations do not warrant generalizations concerning a definite relationship between the degree of ectropion and maldevelopment or some degree of weakness of the tarsus. On the other hand, the tarsal plates act as a skeleton for the lids, accounting for their shape and firmness (36), and it is therefore reasonable to assume that ectropion is related to absence of the tarsus or to some degree of weakness in it.

The second group of cases of congenital ectropion takes the form of eversion of the upper eyelids. The eversion, which is observed immediately after birth and which disappears within days or weeks, apparently occurs during the passage of the child through the birth canal. It is not yet clear whether the associated edema of the palpebral conjunctiva is the result of the eversion, which itself is the result of birth trauma, or the eversion is secondary to a preexisting edema.

Absence or deficiency of the tarsal plates was apparently not a factor in any case in this group, though it was specifically excluded only by Ostriker and Lasky (4) and by Young (14), who reported the single histologic examination of the affected tissues. Only Mertens (13) mentioned an abnormal hereditary anlage as a possible etiologic factor, and he did not pursue the suggestion. There is nothing in the description of his case to support the idea except that the child presented characteristics of mongolism.

THE LITERATURE OF DISTICHIASIS

The literature of congenital distichiasis, which is far more extensive than the literature of congenital ectropion, can be discussed from several different points of view:

1. Status of the tarsus, meibomian glands, and aberrant eyelashes. Although Becker (18), in the first recorded cases of distichiasis, noted that the aberrant cilia emerged immediately beside the orifices of the meibomian glands, Nicati (19), in the second report of the anomaly (the third recorded case), showed by microscopic examination of an

excised specimen that these lashes emerged from the orifices of these glands; he apparently studied only the points from which the aberrant lashes emerged. In his opinion, the meibomian glands were similar to sebaceous follicles, whose structure and function they shared.

Continued investigation of this phase of the anomaly produced widely different findings. In some cases the meibomian glands were rudimentary and undeveloped. Thus in Herrnheiser's (20) case, the first to be studied histologically, a posterior row of cilia in each eyelid replaced the orifices of these glands. The number of aberrant lashes corresponded to the number of glands. No true meibomian glands could be identified and the structures which apparently represented them were only slightly developed. Erdmann (11) found these glands poorly developed in two of his cases; lashes were present in some of the orifices but not in others.

In Von Szily's (28) case. the posterior cilia emerged from the orifices of the meibomian glands. In his detailed histologic studies (37) he observed that these hairy glands were rudimentary. The tarsus was of normal firmness, length and width. These findings are in contrast to Kuhnt's (24) impression that the component tarsal elements in his case were less firm and less closely textured than in cases in which normal meibomian glands are present.

In Landau's (8) case, as in Kuhnt's, hair follicles had apparently taken the place of these glands and occupied their ducts. In Brailey's (25) case, the orifices of the glands were replaced by the openings of follicles of the accessory cilia. Microscopic examination showed the tarsus to be of normal thickness, density, and structure, but there was no trace of meibomian glands or epithelial cells, though the author, as already mentioned, felt that the small size of the specimen did not warrant conclusions.

In some cases, such as Traquair's (26), there was no histologic examination but an apparent but not conclusive clinical absence of the meibomian glands. In other cases, such as that reported by DeVoe and Horwich (17), there was a row of orifices on each eyelid. In their case the tarsal plate felt normal except for accentuation of the concavity.

In some cases, such as Begle's (27), a row of cilia on the inner border of the margin of each lid replaced the orifices of the meibomian glands. Histologic examination revealed the replacement of these glands by hyperplastic sebaceous glands, which discharged into the follicles of well developed accessory cilia. Frolowa (31) found abnormal cilia replacing the orifices of the meibomian glands in the lid margins; when no hairs were present on the posterior border, either no openings were

apparent or there were small openings at distances corresponding to the location of the meibomian glands.

In many of my personal cases the tarsus was either absent on palpation or was small and weak. Its complete absence in the lower lids was established in Cases 1 and 5, when operation was done for correction of an ectropion, and was further confirmed by histologic examination of excised specimens. Both of these patients had some aberrant cilia in the upper lids but none in the lower. It would have been interesting to determine histologically the relation of the posterior cilia in the upper lids to any meibomian glands present, but there was no justification for excision of tissue for examination. In both of these cases tarsal structures were clinically present in the upper lids, in which there was some distichiasis. This is not, however, conclusive evidence; a structure which is normal on clinical investigation may prove undeveloped or otherwise abnormal under the microscope.

The cilia differed widely in the number, appearance, and direction of their shafts. This was evident in my own cases as well as in the literature. Some patients had only a few additional lashes on one or two lids, in areas in which the orifices of the meibomian glands usually open. Others had almost complete accessory rows in all four lids. In Case 3, in which the distichiasis affected only the lower lids, orifices of the meibomian glands were absent, though they were present and apparently normal on the upper lids. No orifices were observed in the other nine cases of distichiasis, even when they were not replaced by aberrant cilia.

In most instances the hairs were pale, thin, and of the lanugo types, though in some cases they were dark and quite similar to the anterior normal row; this was particularly true in the accessory row of lashes in the left upper lid in Case 15.

In most cases some of the posterior lashes rubbed against the cornea and bulbar conjunctiva, producing conjunctivitis, keratitis, and corneal scars. In other cases the hairs were inclined downward along the margin of the affected lid. In Case 15, the aberrant lashes assumed the general direction of the normal anterior lashes and did not touch the eyeball.

2. Combined ectropion and distichiasis. The combination of congenital ectropion and distichiasis was first reported by Erdmann (11). In this case the lids were in normal position but the lower lacrimal points were slightly everted. In Landau's (8) case there was vertical shortening of the upper eyelids, the cutaneous portions of the margins being slightly everted.

The series of cases in the same family which I am reporting show an

apparently unique combination of ectropion and distichiasis. Ten of the affected patients whom I examined personally had distichiasis, which in eight cases was accompanied by ectropion. The ectropion varied from a slight condition affecting only the lower lids to a very marked condition which in two cases affected all four lids. Information obtained about two other members of the family from the surgeon who had operated on them indicated that ectropion was present in all four lids; no information was secured about distichiasis. Another deceased member of the family was reported to have had complete ectropion in all four lids, but distichiasis was not mentioned.

3. Related anomalies. In reported cases of distichiasis the related anomalies took several forms:

"Small and tender" eyes were mentioned by Traquair (26) as a feature of the ocular anomalies on the paternal side of his patient's family. In my own series, all ten members of the family whom I have examined personally had short palpebral fissures horizontally, this anatomic characteristic giving the impression that the eyes were small. The grandmother of the propositus (I, 2) was reported by her sons to have had such eyes, though she apparently had neither ectropion nor distichiasis.

Vertical shortening of the eyelids was present in some of my cases, as in Landau's (8), in which lagophthalmos and slight ectropion of the upper lids accompanied distichiasis. In his report, made in 1947, he revived Fuchs's (5) study, published in 1889, on the relation between the height and vertical extension of the upper eyelids, which Fuchs expressed as a coefficient. With a coefficient below 1.5 (1.9 in older persons), normal closure of the lids is impossible.

In all six of my own cases of distichiasis in which these measurements were made, the coefficient was lower than normal. In three other cases (Cases 10, 13, and 16), no measurements are available, but the fact that the surgeons who operated on these patients found it necessary in each case to use skin grafts to correct the ectropion of all four lids suggests that the lids were abnormally short. In the two cases in which I operated personally (Cases 1 and 5), although the coefficient indicated that the lids were abnormally short, the ectropion present in the lower lids did not seem to be due to any lack of skin but rather to a relaxation produced by absence of the tarsus. For this reason, the Kuhnt-Szymanowski technique was used in each instance.

4. Other ectodermal defects. Braley (35) and Halberg and Paunessa (34) reported mandibulofacial dysostosis, a syndrome caused by congenital arrest of the primitive ectoderm (35), in association with dis-

tichiasis. The two accessory bicuspid teeth present in Brailey's (25) case are also evidence of an ectodermal defect. In Case 2 of my own series, in which distichiasis was present without ectropion, the patient had been operated on in childhood for congenital cataracts. In Case 4 the eyes were normal, but the child was a moron, possibly because of some ectodermal cerebral defect.

5. Anatomic defects producing ectropion and distichiasis. Ectropion and distichiasis apparently have some anatomic defect as their common background. This is suggested by some of my own cases, in which the same patient presented both anomalies, sometimes in different lids and sometimes in the same lid. The cause of both conditions seems to be a defect of tarsal development. Vertical shortness of the eyelids is probably also due to a deficient development of all the tissues in the lids secondary to primary absence or deficiency of the tarsus.

Two chief theories have been advanced to explain the occurrence of distichiasis. Kuhnt (24), arguing from histologic evidence, concluded that it is a heterotopic abnormality in which the meibomian glands are replaced by true cilia with characteristic adnexa. Brailey (25) concurred. Erdmann (11), who, like Herrnheiser (20), found poorly developed meibomian glands in his specimen, took issue with Kuhnt. His assumption was that in distichiasis, the anlage in which both meibomian glands and cilia develop does not differentiate, with the result that the development of the acini of the meibomian glands is rudimentary and a rudimentary eyelash also develops.

The second theory, that distichiasis may be an atavistic phenomenon in which glands of a highly modified type fail to develop and are replaced by similar structures which are more primitive phylogenetically, was first advanced by Begle (27). In his case, meibomian glands were replaced by hyperplastic sebaceous glands discharging into the follicles of well developed accessory cilia. In Von Szily's (37) opinion, in which Frolowa (31) concurred, congenital distichiasis is merely a return, in part, to a phylogenetically earlier form. Both anatomic and morphological studies indicated to him that this anomaly is a true idiotypical recessive hereditary deformity; that the posterior row of cilia is not merely a displaced row but one which has the characteristics of rudimentary hairy meibomian glands; and that these glands most probably represent phylogenetically intermediate stages of the series of transformations through which ordinary hairs have passed in the ancestors of present day mammals in their development into meibomian glands.

Blatt (29) also accepted the atavistic theory of origin. It is possible, he argued, that some disorder in the germinal layer may inhibit de-

velopment of the gland, with the result, since the primary germinal layer is the same for both glands and hair, that hair is formed. This argument is in line with the general opinion that disordered development is determined in the germinal layer in congenital distichiasis because of its familial occurrence and because it is assumed that true normal meibomian glands originate from the hair anlage of the tegument of the lid margin. Like Von Szily, Blatt regarded hairy glands as a physiologically lower type which was replaced, in course of time, by the higher type normal meibomian glands.

Frolowa's (31) findings may explain the different histologic data reported by various observers; in her case she found not only rudimentary glands with cilia, some of which resembled ordinary sebaceous glands, but also glands with the structure of normal meibomian glands. It is quite possible that the different histologic findings which have been reported by different observers may be explained, on this basis, as regressions to any one of several different stages, from true cilia, through rudimentary hairy glands, to true meibomian glands. Da Pozzo (33) also found both normal and rudimentary meibomian glands in one of his cases.

The chief objection to the atavistic theory of human aberrations is that modern embryologists are extremely loath to accept it. On the contrary, they lean toward the belief that such changes are either true or specific mutations.

6. Hereditary influence and mode of inheritance. The possible hereditary factor in distichiasis was first mentioned by Wood (21), whose two cases occurred in a father and daughter. Westhoff (23) also reported the condition in two generations (the patient, his mother, his brother, and his maternal uncle). In Frolowa's (31) case the condition was present in a father and his only son. Da Pozzo (33) reported the condition in a mother and one of her sons, and in the case reported by DeVoe and Horwich (17), the condition was present in the patient's sister.

Erdmann (11) first reported distichiasis in three generations (grandmother, mother, and daughter; the anomaly was not present in two siblings in the third generation). Blatt's (29) contribution is particularly important from the standpoint of the hereditary factor: Five members of three generations of the same family were affected (the grandmother, a son, a daughter, and two sons of the son); a daughter of the daughter was not affected. These five cases indicate autosomal dominant inheritance. They are the first cases to be reported showing the affection in both sexes in three generations, although those affected in the third generation consisted of two sons of an affected son.

Waardenburg (38) some years ago expressed the opinion that hereditary findings in the cases of distichiasis reported in the literature are suggestive of dominance because of the true rarity of the condition, which he thought might possibly be polyhydridism.

The pedigree (Figure 1) of the family which I have studied gives evidence of a dominant autosomal inheritance of both ectropion and distichiasis, there being direct transmission of both conditions over three generations. The possibility of sex linkage of the pathogenic gene is eliminated by the absence of predilection for either sex in any of the generations. If there were sex-linked dominant *X* chromosomal inheritance, none of the sons of the affected fathers would show the condition, as some of them do.

The affected parents' genotype for the pathogenic gene is apparently heterozygous. In the first branch of the family, while the father was affected, 50 percent of his offspring were not. The large number of offspring in this family provided the opportunity to observe that four of the affected parents in the three generations had affected sons and daughters but that three of the four also had normal sons or daughters.

The pathogenic gene in this series of cases showed a high degree of penetrance. This is evident in the fact that more than half of the members of the family presented one defect or the other, or both. The expression of the pathogenic gene is somewhat variable, because the degree of ectropion or distichiasis shows considerable variance. There is no doubt of the expression, however, since of the ten patients examined, only two showed distichiasis alone. The other eight showed both ectropion and distichiasis.

SUMMARY

This thesis is based on the investigation of a family of eighteen members in three generations, eleven of whom suffered from congenital ectropion, in eight instances associated with distichiasis. Two had distichiasis alone, and only five had normal eyes.

Ectropion and distichiasis are very rare congenital anomalies of the lids, as is shown by an extensive review of the literature. Previously reported cases of ectropion, numbering five at most, lack many of the characteristics of the cases in this family. The association of ectropion and distichiasis, reported in two cases at most, also lacks many of the characteristics of the cases in this family.

Histologic examination of specimens of two cases in this family showed absence of meibomian glands and either absence of the tarsal plates or the presence of only vestigial structures. This etiologic factor

was not determined in the cases of ectropion previously reported. Absence, weakness, or some other deficiency of the tarsus was determined by palpation in the other affected cases, but such an examination cannot be regarded as conclusive.

Other characteristic features of this syndrome of congenital ectropion and distichiasis included narrowing of the palpebral fissures horizontally (described by the patients as "small eyes") and vertical shortness of the lids.

The mode of inheritance of this congenital syndrome in the family under investigation was evidently of an autosomal dominant type.

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